Malignant hyperthermia involving the administration of desflurane

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Purpose: This report describes an episode of malignant hyperthermia (MH) in a ten year old boy receiving desflurane anaesthesia.

Clinical features: Following induction of general endotracheal anaesthesia with thiopentone and succinylcholine, desflurane was administered for maintenance of anaesthesia. Ten minutes after commencing desflurane administration, heart rate and PETCO₂ increased to 165 bpm and 50 mmHg, respectively. Initially, the tachycardia was attributed to a sympathetic response secondary to desflurane. Desflurane was discontinued and isoflurane was started. Minute ventilation was increased to decrease PETCO₂. Over the next five minutes, temperature increased to 38.4°C as the PETCO₂ increased to above 60 mmHg. Venous and arterial blood gases were drawn which showed acidosis and hypercapnia. Temperature and PETCO₂ continued to increase, reaching peak values of 41°C and 77 mmHg, respectively. Efforts to cool the patient were made. A total of 220 mg dantrolene sodium was administered iv. Following dantrolene, the temperature increase and acidosis subsided. Heart rate and PETCO₂ decreased to 130 bpm and 36 mmHg, respectively. The surgical procedure was expeditiously performed. Postoperatively, in the Paediatric Intensive Care Unit, a dantrolene infusion of 20 mg·hr⁻¹ was administered for 12 hr. The trachea was extubated the following morning. Several days later, the patient underwent another surgical procedure without complications using MH-safe anaesthetics.

Key words

ANAESTHESIA: paediatric;

ANAESTHETICS, VOLATILE: desflurane;

COMPLICATIONS: malignant hyperthermia.

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Conclusion: Onset of tachycardia in a patient receiving desflurane may initially be attributed to desflurane-induced sympathetic hyperactivity. This poses a clinical challenge in the diagnosis of MH during desflurane anaesthesia.

Objectif: Communiquer le compte rendu d'un épisode d'hyperthermie (HM) survenu chez un enfant de dix ans anesthésié au desflurane.

Caractéristiques cliniques: Après l'induction d'une anesthésie générale endotrachéale avec du thiopentone et de la succinylcholine, du desflurane a été administré pour l'entretien de l'anesthésie. Deux minutes après le début de l'administration de cet agent, la fréquence cardiaque et le PETCO₂ ont respectivement augmenté à 165 bpm et 50 mmHg. Initialement, la tachycardie a été attribuée à une réaction sympathique provoquée par le desflurane. Pendant les cinq minutes suivantes, la température a augmenté à 38,4°C et la PETCO₂ a dépassé 60 mmHg. Des échantillons de sang artériel et veineux ont révélé la présence d'acidose et d'hypercapnie. La température et la PETCO₂ ont continué d'augmenter à des valeurs maximales respectives de 41°C et 77 mmHg. Des manoeuvres de refroidissement ont été entreprises. Une dose totale de 220 mg de dantrolène sodique a été administrée par la voie veineuse. La température et l'acidose se sont stabilisées. La fréquence cardiaque et la PETCO₂ ont baissé respectivement à 130 bpm et 36 mmHg. L'intervention a été terminée rapidement. En postopératoire, à l'unité des soins intensifs pédiatriques, une perfusion de dantrolène 20 mg·h⁻¹ a été administrée pendant 12 h. La trachée a été extubée le lendemain matin. Quelques jours plus tard, le patient a subi une autre intervention chirurgicale sous anesthésie ne comportant pas d'agents déclenchants de l'HM.

Conclusion: Sous desflurane, il est possible d'attribuer un accès de tachycardie à l'hyperactivité sympathique. Ceci peut compliquer le diagnostic de l'HM.

Desflurane is a relatively new inhalational anaesthetic that is structurally related to isoflurane and enflurane. Tachycardia may follow desflurane administration as a result of activation of the sympathetic nervous system.¹ Elevation in heart rate may also be a hallmark for malig-

nant hyperthermia (MH). Episodes of MH in humans receiving desflurane have not been described in the literature. The following report describes an episode of tachycardia and hyperthermia in a patient who received desflurane.

Case report

A 10-yr-old, 50 kg boy was involved in a motor vehicle accident and sustained fractures of the mandible and right tibia. In the emergency room, the vital signs were: heart rate 84 bpm, blood pressure 142/86 mmHg, room air oxygen saturation (SpO_2) 97%, and temperature 37°C. Room air arterial blood gas showed: pH 7.35, PCO_2 42, PO_2 87, bicarbonate 23 $\text{meq} \cdot \text{L}^{-1}$, and base deficit 2 $\text{meq} \cdot \text{L}^{-1}$. Other laboratory values include: potassium 3.4 $\text{meq} \cdot \text{L}^{-1}$, carbon dioxide 26 $\text{meq} \cdot \text{L}^{-1}$, and haemoglobin 16.0 $\text{g} \cdot \text{dL}^{-1}$. Several hours later, the patient was taken to the operating room for emergency fasciotomy of the right lower extremity and open reduction internal fixation of the right tibia. In the initial preoperative evaluation, the patient's family history was unknown in view of the fact that the patient was adopted.

In the operating room, the patient was preoxygenated using a circle anesthesia system with a soda lime CO_2 absorber. The vital signs prior to induction of general anaesthesia were as follows: heart rate 84 bpm, blood pressure 146/96 mmHg, SpO_2 100%, and PETCO_2 30 mmHg. A rapid sequence induction with cricoid pressure was performed with thiopentone 150 mg, fentanyl 100 μg , and succinylcholine 80 mg. A 5.5 mm cuffed endotracheal tube was placed nasally without difficulty under direct laryngoscopy with Magill forceps. Although no evidence of masseter spasm was observed, the fractured mandible made this determination difficult.

After tracheal intubation, heart rate and blood pressure increased to 125 bpm and 155/98 mmHg, respectively and PETCO_2 was 35–40 mmHg. Initially, 6% desflurane was administered. Several minutes later, desflurane concentration was increased to 10%. After ten minutes of desflurane administration, heart rate and PETCO_2 increased to 165 bpm and 50 mmHg, respectively. Blood pressure and end-tidal desflurane concentration was 136/76 mmHg and 10%, respectively. At this juncture, the tachycardia was attributed to either hypercapnia or desflurane-related sympathetic hyperactivity.

Desflurane administration was discontinued and isoflurane administration was started. The anaesthesia team investigated the aetiology for the hypercapnia. Minute ventilation was increased and no pattern suggestive of obstruction or rebreathing was observed with the PETCO_2 waveform. There was no exhaustion of the soda lime CO_2 absorber. An oesophageal temperature probe was inserted at this time, which gave a reading of 37°C.

Over the next five minutes, PETCO_2 and temperature increased to 60 mmHg and 38.4°C, respectively. A venous blood gas was first obtained which showed: pH 7.07, PCO_2 82 mmHg, PO_2 48 mmHg, bicarbonate 23 $\text{meq} \cdot \text{L}^{-1}$, and base deficit 7 $\text{meq} \cdot \text{L}^{-1}$. We diagnosed an MH reaction and instituted therapy including: (1) discontinuation of nitrous oxide and isoflurane, (2) hyperventilation with 100% oxygen using an MH "clean" anaesthesia machine (3) application of ice bags to the exposed skin surfaces, (4) gastric lavage with iced saline, (5) intravenous infusion of cold normal saline, and (6) administration of a total of 220 mg dantrolene sodium over the next 30 min.

During the hyperthermic episode, systolic blood pressure was approximately 100 mmHg and SpO_2 varied between 98–100%. Heart rate was 150–160 bpm. Before a response to dantrolene could be appreciated, temperature and PETCO_2 reached peak values of 41°C and 77 mmHg, respectively. After 2.5 $\text{mg} \cdot \text{kg}^{-1}$ dantrolene, temperature and PETCO_2 decreased to 40°C and 50 mmHg, respectively. Another dose of 2 $\text{mg} \cdot \text{kg}^{-1}$ dantrolene was administered, resulting in a decrease in heart rate to 130 bpm. Temperature and PETCO_2 decreased to 38°C and 36 mmHg, respectively. An arterial blood gas drawn prior to dantrolene administration showed: pH 7.16, PCO_2 65 mmHg, PO_2 401 mmHg, bicarbonate 23 $\text{meq} \cdot \text{L}^{-1}$, base deficit 7 $\text{meq} \cdot \text{L}^{-1}$. Laboratory values from chemistry and haematology profiles drawn simultaneously were: potassium 7.1 $\text{meq} \cdot \text{L}^{-1}$, carbon dioxide 19 $\text{meq} \cdot \text{L}^{-1}$, anion gap 19 $\text{meq} \cdot \text{L}^{-1}$, and haemoglobin 6.5 $\text{meq} \cdot \text{dL}^{-1}$. Dextrose and insulin were administered to treat hyperkalaemia. Mannitol and furosemide were given to promote diuresis. A total of 3700 ml crystalloid and one unit of packed red blood cells were administered. The urine was clear, yellow and the intraoperative urine output was 1100 ml. Following dantrolene therapy, arterial blood gas values were: pH 7.36, PCO_2 36 mmHg, PO_2 236 mmHg, bicarbonate 24 $\text{meq} \cdot \text{L}^{-1}$, base deficit 1 $\text{meq} \cdot \text{L}^{-1}$. Serum chemistry values were: potassium 4.6 $\text{meq} \cdot \text{L}^{-1}$, carbon dioxide 24 $\text{meq} \cdot \text{L}^{-1}$, anion gap 7 $\text{meq} \cdot \text{L}^{-1}$.

During the anaesthetic management of the hyperthermic episode, the surgeons completed the fasciotomy in an expeditious manner. The patient was subsequently taken to the Paediatric Intensive Care Unit and the trachea remained intubated overnight and a dantrolene infusion was administered at a rate of 20 $\text{mg} \cdot \text{hr}^{-1}$ for 12 hr.

Myoglobin appeared in the urine on postoperative day one. The highest serum creatinine phosphokinase (CPK) level reached was 28,314 $\text{U} \cdot \text{L}^{-1}$, measured on the morning of postoperative day one. This is in comparison with the CPK levels drawn in the emergency room and in the operating room which were 1325 and 6918 $\text{U} \cdot \text{L}^{-1}$,

respectively. The trachea was extubated on postoperative day one with no evidence of neurological sequelae. The patient subsequently received oral dantrolene at a dose of 100 mg, four times a day for three days. Several days later, the patient underwent another surgical procedure without complications using MH-safe anaesthetics.

Further investigation of the patient's biological family history revealed that the paternal uncle died during hip surgery at the age of 25 yr, allegedly from malignant hyperthermia. A geneticist evaluated the patient and recommended that the patient and family members have serum drawn to measure levels for CPK, LDH, and aldolase several months after discharge. Based on these test results, a future decision would be made regarding muscle biopsy testing. However, the patient was lost to further followup.

Discussion

Two studies by Wedel *et al.*^{2,3} have shown that desflurane triggers malignant hyperthermia in swine. In their first study, two of the six purebred MH-susceptible swine did not develop MH when exposed to two MAC desflurane for one hour. They hypothesized that desflurane may not be as strong a triggering agent as other volatile inhalational agents. In their second study, the fastest onset of an MH episode occurred with exposure to halothane when compared with isoflurane and desflurane.

Halothane has been reported to trigger MH in humans without the administration of other anaesthetic triggering agents.⁴ In the several published reports⁵⁻⁷ of malignant hyperthermia in humans associated with isoflurane anaesthesia, succinylcholine was also administered. To date, malignant hyperthermia associated with desflurane anaesthesia in humans has not been described. According to the registry of the Malignant Hyperthermia Association of the United States (MHAUS), there have been several cases of MH associated with desflurane anaesthesia. The first desflurane-related episode reported to MHAUS was in 1993. According to the MHAUS registry, our report is one of three desflurane-related episodes to occur in 1994. During this episode, hard copy printouts revealed that when the PETCO₂ reached 77 mmHg, the end-tidal desflurane concentration was 10%. Since succinylcholine was also administered, the development of malignant hyperthermia in this patient cannot be solely attributed to desflurane.

Tachycardia is often an initial presenting sign in the development of MH. Before making the diagnosis of MH, the anaesthesia team investigated other causes of tachycardia such as hypercapnia, hypovolaemia, and light depth of anaesthesia. Desflurane anaesthesia is

unique in that tachycardia and hypertension can occur secondary to sympathetic hyperexcitation, which does not occur with isoflurane anaesthesia.¹ The hypercapnia that accompanies MH also stimulates the sympathetic nervous system. Therefore, the diagnosis of MH in a patient receiving desflurane may be difficult. One clinical feature that may differentiate MH from desflurane-induced sympathetic hyperactivity is the transient nature of sympatho-excitation, while in MH the hypercarbic response may be overwhelming. Increasing the desflurane concentration from 1.0 to 1.5 MAC has been shown to produce sympatho-excitation in healthy, young volunteers.¹ However, as the desflurane concentration was increased from 6% to 10% in this patient, an increase in heart rate was observed without a concomitant rise in blood pressure. Haemorrhage and hypovolaemia may have accounted for the occurrence of tachycardia without hypertension, as evidenced by the decrease in serum haemoglobin from 16.0 to 6.5 g·dl⁻¹, intraoperatively.

Since muscle biopsy testing was not undertaken to confirm the diagnosis of MH in this patient, clinical criteria must be used to assess the likelihood of an MH reaction. Etiologies other than MH may account for the clinical presentation. For example, tachycardia may be explained on the basis of hypovolaemia, hypercapnia, and desflurane-induced sympathetic discharge. Hypercapnia may be attributed to inadequate ventilation, while elevation of CPK levels and myoglobinuria may be explained on the basis of motor vehicle accident trauma. But, the combination of hyperthermia (peak temperature of 41°C), acidosis, base deficit, hyperkalaemia, myoglobinuria, and elevated CPK levels support the clinical diagnosis of MH in this patient. The dramatic response to 4.5 mg·kg⁻¹ dantrolene, during surgery, also favours the likelihood of an MH reaction. Moreover, the clinical features of this patient were similar to that of the patients described by Kolb *et al.*⁸ to have probable or unequivocal MH.

In the Paediatric ICU, a dantrolene infusion was started. We acknowledge that a dantrolene infusion may not be the optimal approach for postoperative management, following an acute MH episode. Flewellen *et al.*⁹ showed that following bolus administration of dantrolene, near steady state levels exist for almost six hours with an elimination half-time of 12 hr. Based on these findings, acute bolus intravenous administration will achieve therapeutics, without the need for a continuous infusion. Therefore, caution must be taken to avoid side effects such as nausea, muscle weakness, altered sensorium and phlebitis.

This episode serves as a reminder that desflurane is capable of triggering MH, especially when used in com-

bination with succinylcholine. The onset of tachycardia may initially be attributed to the sympathetic hyperexcitation properties of desflurane. This poses a challenge to the clinician in the diagnosis of MH during desflurane anaesthesia.

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